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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,274	12/19/2005	Toshihiko Kakiuchi	1110-0339PUS1	5695

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EXAMINER	
HUANG, GIGI GEORGIANA	

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
05/01/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/561,274	KAKIUCHI, TOSHIHIKO	
	Examiner	Art Unit	
	GIGI HUANG	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-9 and 12-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-9 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The response filed February 19, 2008 has been received, entered and carefully considered. The response affects the instant application accordingly:

   a. Claims 1-6 and 10-11 have been cancelled.

   b. Claims 12-15 have been added.

2. Claims 7-9 and 12-15 are pending in the case.

3. Claims 7-9 and 12-15 are present for examination.

4. The text of those sections of title 35.U.S. Code not included in this action can be found in the prior Office action.

5. All grounds not addressed in the action are withdrawn or moot.

6. New grounds of rejection are set forth in the current office action.

Claim Rejections - 35 USC § 112

7. Claims 14-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection to the newly added claims 14-15.

Claims 14-15 draw to a method of treating varicose veins of lower extremities comprising administering a composition consisting essentially a therapeutic effective amount of EPA ethyl ester, other inactive fatty acids, tocopherol, and optionally a

pharmaceutical carrier; wherein the eicosapentaenoic acid ethyl ester is present in an amount of at least 85% by weight, based on the total weight of the composition of fatty acids in the composition; and wherein said eicosapentaenoic acid ethyl ester is orally administered at a dosage amount of 0.1 to 9 g/day.

There is support for the content of EPA to be preferably at least 85% by weight of the total fatty acids in the composition.

The term "other inactive fatty acids" fail to be properly described in the specification to in a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is directed to fatty acids that have no activity whatsoever or are neutral. As fatty acids are not neutral (they are acids) and are known to have chemical and biological activity, there is no description present as to what "other inactive fatty acids" means, nor what would constitute an "inactive fatty acids".

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 14-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14-15 draw to a method of treating varicose veins of lower extremities comprising administering a composition consisting essentially a therapeutic effective amount of EPA ethyl ester, other inactive fatty acids, tocopherol, and optionally a

pharmaceutical carrier; wherein the eicosapentaenoic acid ethyl ester is present in an amount of at least 85% by weight, based on the total weight of the composition of fatty acids in the composition; and wherein said eicosapentaenoic acid ethyl ester is orally administered at a dosage amount of 0.1 to 9 g/day.

The claims are indefinite as it is unclear what constitutes “other inactive fatty acids”. It does not allow one of skill in the art to know the metes and bounds of the invention. For purposes of prosecution, it will be takes to mean any fatty acid.

10. Claims 14-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 14-15, the phrase “optionally a pharmaceutical carrier " renders the claim indefinite because it is unclear whether the limitations of pharmaceutical carrier following the phrase are part of the claimed invention. It does not allow one of skill in the art to ascertain the metes and bounds of the invention.

11. Claims 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. In the present instance, claims recites the broad recitation “comprising administering”, and the claim also recites “consisting essentially of” which is

the narrower statement of the range/limitation. For purposes of examination, the term "comprising" is open and supersedes the term "consisting essentially of", which is predominately open, the claims as written will be viewed as open language.

Additionally, claims 12-13 recite a composition consisting essentially of an effective amount of EPA ethyl ester and a pharmaceutically acceptable carrier, but further recites a proportion of the EPA ethyl ester relative to other fatty acids present in the composition. This is indefinite as other fatty acids would be other actives which would be contrary to the limitation of EPA ethyl ester as the only active recited. The claims are indefinite and do not allow one of skill in the art to ascertain the metes and bounds of the invention.

12. Claim 13 recites the limitation "tocopherol" in claim 12. There is insufficient antecedent basis for this limitation in the claim. Tocopherol has biological activity and as written is an active agent.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 12-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Bruzzese (U.S. Pat. # 5,776,978).

Bruzzese teaches a composition comprising EPA and/or DHA in their fatty acid, ester, and salts forms for use in the prevention and/or treatment of arthrosclerosis, nervous system, cardiovascular, skin, and malignant pathologies (Abstract, Col. 1, lines 5-22).

Bruzzese teaches compositions comprised of EPA esters or EPA ethylesters and 10-40% by weight of antioxidant/reducing vitamins or provitamins. Examples included DHA esters and compositions comprised of EPA esters or EPA ethylesters. Bruzzese teaches that it is understood that DHA and EPA in any of the form taught can be used individually or as a mixture of the two. The mixtures can be prepared by combining the desired quantities of the purified forms or the mixtures of the desired esters or salts thereof (Col 1, lines 5-15, 27-35, 39-47, Col. 3, Table 1, Col. 5, Example 4, Col. 6, Example 5 and 6, Claims 1-7).

Bruzzese teaches compositions where the optimal quantity of DHA and EPA, acid, esters, and salts can be combined with reducing vitamins, and placed in soft gelatin capsules using conventional techniques (Col.4, lines 56-68). Several forms are exemplified at the optimal amounts of 300mg of EPA salt (Example 3), and 1000mg of EPA (acid), and ethyl ester forms of DHA (Example 5). The EPA ethylester would have been immediately envisioned as taught by Bruzzese at similar doses. The amounts are optimized and would be expected to be give once a day, but if give several times a day, the doses still fulfill the claims.

Bruzzese also taught the use of these compositions for cardiovascular conditions and atherosclerosis, which encompasses varicose veins (see Mayo Clinic sheets scope

of cardiovascular disease/conditions in the art) anticipating Claim 6 of the instant application.

All the critical elements are taught by the cited reference and thus the claims are anticipated.

15. Claims 12-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Horrobin (U.S. Pat. # 5604216).

Horrobin teaches a pharmaceutical and nutritional composition comprising cholesterol fatty acid ester in a suitable diluent or carrier. The cholesterol fatty acid esters taught include those formed from eicosapentaenoic acid. Horrobin teaches that the ester forms are desirable as they are usually stable and resistant to oxidation compared to the fatty acids themselves, salts, or triglyceride forms. Horrobin teaches that fatty acids including EPA have therapeutic value in a number of disorders specifically addressing the cardiovascular system and peripheral arterial disease which encompasses varicose veins (see Mayo Clinic sheets scope of cardiovascular disease/conditions in the art).

Horrobin teaches that the significance is in the context of delivering these fatty acids by administering the in the form of esters for the treatment of any of the disclosed conditions and any other disease. Horrobin teaches the synthesis of the esters and that they can be administered orally, topically parenterally, and any other appropriate route. The forms included tablets, capsules, emulsions, other pharmaceutical dosage forms, foods, and skin care preparations (cosmetics). The doses for oral administration are preferably from 500mg to 10g of the cholesterol ester per day. Horrobin also teaches

soft gelatin capsules at several dosages (100, 250, 500, 750mg) of cholesterol-EPA (ester) in capsule form (soft and hard) among others (Abstract, Col. 1, lines 10-30, Col. 2, lines 18-27, 37-65, 68, Col. 3, lines 1-4, 35-61, Col. 5, lines 25—45, Col. 6, Example 3, lines 55-68, Col. 7, lines 5-14, 25-45, Claims 1,2, and 9).

All the critical elements are taught by the cited reference and thus the claims are anticipated.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 9 and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kiliaan et al. (WO 01/84961) in view of Oouchi et al. (JP 06-092847).

A machine translation is submitted for Oouchi et al. and document references are to the translation.

Kiliaan et al. teaches a composition comprised of long chain polyunsaturated fatty acids, preferably eicosapentaenoic acid, for use of vascular disorders.

Kiliaan teaches that the composition can comprise solely the omega-3 fatty acids (preferably EPA or DHA), only omega-6 fatty acids, or a combination (Page 6, Lines 9-15). Kiliaan et al. also teaches the composition to have best results when EPA is mixed with docosahexaenoic acid (DHA) for the long chain polyunsaturated fatty acids, but allows for them to be utilized singularly (claims 1, 4 and 5). When used singularly in a

composition solely of omega-3 fatty acids, EPA would constitute at least 85% by weight of the total fatty acids in the composition, as it would be the only fatty acid. The fatty acids can be free, bound to a suitable backbone, or esterfied (Page 6, lines 10-15, Page 7, lines 25-30). The composition can be a dietetic, pharmaceutical, and a nutritional preparation.

Kiliaan teaches the daily dose of the preparation in particular contains at least 50mg of EPA and preferably 50 to 1000mg. Kiliaan also teaches that the per daily dose of the preparation for long chain poly unsaturated fatty acids utilized (i.e. EPA) is at least 120 mg (Page 7, lines 1-5, Page 11, lines 8-15).

The product forms could be a liquid, powder, bar, cookie, sweet, concentrate, paste, sauce gel, emulsion, tablet, capsule for providing a daily dose either as a single or multiple dose form. The products would be packaged by methods know in the art to keep the products fresh for easy use, administration, and shelf life (Abstract, Page 5, lines 23-32, Page 6, lines 1-9, 24-28).

The uses for the compositions are for the treatment of vascular, cardio-and cerebrovascular disorders and a selected range of secondary problems. Specific cardiovascular problems that were addressed were thrombi, vascular accidents, atherosclerosis, and varicose veins/varices (Page 11, lines 28-30, Page 12, lines 9-14).

Kiliaan et al. does not expressly teach the use of eicosapentaenoic acid ethyl ester.

Oouchi et al teaches that ethyl all- cis-5,8,11,14,17-icosapentaenoate (eicosapentaenoic acid ethyl ester) is preferable over eicosapentaenoic acid as it has

less toxicity particularly when given orally. Eicosapentaenoic acid is acidic and can stimulate the membrane, the salt forms can have excessive ingestion of the salt with long term use, but the eicosapentaenoic acid ethyl ester (EPA-E) does not have these concerns, has excellent safety and very few side effects (Abstract, Paragraph 26-27).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute eicosapentaenoic acid ethyl ester for eicosapentaenoic acid, as suggested by Oouchi et al., and produce the instant invention. It would be obvious to one of skill in the art to utilize a recognized form such as eicosapentaenoic acid ethyl ester with reduced side effects and high safety, for the composition as Kiliaan teaches the usefulness of esterified forms of eicosapentaenoic acid for the composition.

One of ordinary skill in the art would have been motivated to do this because it is always desirable to utilize the form of the active desired with the least amount of side effects and highest level of safety to avoid dangerous or negative results for the administered composition during use.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the

time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

18. It is noted and appreciated Applicant's attempt to address the inclusion of tocopherol. While the argument is moot as claims 1-4, 6, and 10-11 are cancelled, Applicant should be aware that the argument is not commensurate in scope with the claims as written.

19. Claims 7-11 rejected under 35 U.S.C. 102(b) as being anticipated by Kiliaan et al. (WO 01/84961).

Claims 10-11 are cancelled, the rejection is moot.

Applicant's argument is persuasive for claim 9 and is subject to a new ground of rejection as addressed above.

Applicant's arguments filed 2/19/2008 have been fully considered but they are not persuasive for claims 7-8. Applicant's argument is not commensurate in scope with the claims and the assertion the Kiliaan does not supply data for the effectiveness for varicose vein is not persuasive as the art teaches the limitations of the claims for the use for thrombi, vascular accidents, atherosclerosis, and varicose veins/varices and the composition limitations. As the art teaches the usefulness for the composition for the condition claimed, the limitations are met.

Accordingly, the rejection of claims 7-8 under 35 U.S.C. 102(b) as being anticipated by Kiliaan et al. (WO 01/84961) is maintained.

20. Claims 7-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Bruzzese (U.S. Pat. # 5,776,978).

Claims 10-11 are cancelled, the rejection is moot.

Applicant's arguments filed 2/19/2008 have been fully considered but they are not persuasive for claims 7-9. Applicant's argument is not commensurate in scope with the claims as the claims are open to other components. Applicant's argument that Bruzzese does not supply data is not persuasive as the art does not need to supply data, only the general teaching of the composition and its uses.

Accordingly, the rejection of claims 7-9 under 35 U.S.C. 102(b) as being anticipated by Bruzzese (U.S. Pat. # 5,776,978) is maintained.

21. Claims 1-4, 6-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Horrobin (U.S. Pat. # 5604216).

Claims 1-4,6, and 10-11 are cancelled, the rejection is moot.

Applicant's arguments filed 2/19/2008 have been fully considered but they are not persuasive for claims 7-9. Applicant's argument is not commensurate in scope with the claims as the claims are open to other components. Applicant's argument that Horrobin does not provide a specific example is not persuasive as the art does not need to provide a specific example, only the general teaching of the composition and its uses.

Accordingly, the rejection of claims 7-9 under 35 U.S.C. 102(b) as being anticipated by Horrobin (U.S. Pat. # 5604216) is maintained.

Conclusion

22. Claims 7-9 and 12-15 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GIGI HUANG whose telephone number is (571)272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fredrick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GH
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Primary Examiner, Art Unit 1612